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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/859,701 | 05/16/2001 | Benjamin P. Warner | S-94,661 | 4132 |
| 35068 | 7590 | 09/15/2006 | EXAMINER | |
| LOS ALAMOS NATIONAL SECURITY, LLC LOS ALAMOS NATIONAL LABORATORY PPO. BOX 1663, LC/IP, MS A187 LOS ALAMOS, NM 87545 | | | DAVIS, DEBORAH A | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1655 | |

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/859,701

Applicant(s)

WARNER ET AL.

Examiner

Deborah A. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2006.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-20 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on June 26, 2003 has been entered.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 1-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pirrung et al (WO 90/15070) in view of Chia-Gee Wang (USP#4,436,826) and Yorkin (USP#4,436,826).

Pirrung et al teaches a method and device for preparing desired sequences on a substrate at known locations wherein bound material of the substrate is exposed to irradiation (pg. 10, lines 1-35) so as to activate material and permit binding (see

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abstract). The substrate has a variety of uses such as screening large numbers of peptides or receptors, wherein receptors are labeled with fluorescent markers for detection. In an alternative embodiment the surface may comprise of cage binding members that are capable of immobilizing receptors in predefined regions of a substrate for selective activation that allow receptors that have differential affinity for one or more ligands to react (pg. 55, lines 30-37 and pg. 56, lines 1-11). A specific binding substance having a strong binding affinity for the binding member and a strong affinity for the receptor or a conjugate of the receptor may be used to act as a bridge between binding members and receptors if desired. The method uses a receptor prepared such that the receptor retains its activity toward a particular ligand (pg. 56 lines 30-36). Steps (a) and step (d) of claim 11 are slightly different in that they recite a negative limitation. Step (a) requires that at least one potential binder is not labeled with an additional optically fluorescent tag. The reference of Pirrung teaches step (a), wherein a screening process for one or more receptors on a substrate that are exposed to labeled antibody binders and detected by photon detection (column 5, lines 14-25). The antibody binder is not labeled with any additional optically fluorescent tags. The reference of Pirrung teaches step (d) of claim 11 wherein the presence or absence of a binding event between the receptors and ligands are detected (page 41, lines 5-10). According to Pirrung et al, receptors used in this method could be organic compounds such as polymers (oligomer), nucleic acids, peptides, drugs, cellular membranes, cells, etc. (pg. 11, lines 7-24). The binder molecule can be selected from the group consisting

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of agonists and antagonists for cell membrane receptors, oligonucleotides, nucleic acids, proteins, antibodies, etc. (pg. 9, lines 30-37).

The method of Pirrung et al is silent with respect to X-ray fluorescence for analysis.

The cited reference of Wang beneficially teaches an immunoassay method for evaluating antigen and antibody binding with X-ray fluorescence (see for example abstract, Figure 2, and column 2). Figure 2 of the cited reference discloses that X-ray fluorescence is the preferred detector for detection of antigen and antibody binding (see for example column 2, lines 60-61). Metal ions serving as the tagging elements (i.e. binders), can be used to detect binding, as claimed (see for example column 5, lines 47-63).

It would have been obvious to one of ordinary skill in the art to select or include x-ray fluorescence in the detection methods of Pirrung, as taught by Wang because different target antigens or antibodies can be assayed simultaneously by employing different tagged mobile units and the mobile units with the tagging elements can be recovered for disposal or for reuse (see for example abstract).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of the evidence to the contrary.

Response to Arguments

1. Applicant argues that the reference of Pirrung does not teach or suggest using X-ray fluorescence detection to detect a binding event. This argument have been considered but not found to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The reference of Pirrung was not relied on for its teaching of X-ray fluorescence detection, the reference of Yokhin was relied on for the teaching of X-ray fluorescence. If the reference of Pirrung taught X-ray fluorescence, it would be applied as a 102 reference.

2. Applicant argues that there is not motivation to combine the reference of Pirrung and Yorkin and that the motivation must come from the references and not from the examiner.

In response, the motivation to combine the references of Pirrung and Yorkin came from the reference of Yorkin (see previous rejection). In addition, the motivation does not have to come from the cited references, but from the knowledge generally available to one of ordinary skill in the art. X-ray fluorescence is known in the art for evaluation of compositions. The examiner takes note that Yorkin does not teach X-ray

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detection of binders, but this argument is moot in view of the newly applied reference of Chia-Gee Wang who teaches X-ray fluorescence in detecting binders (i.e. antigen and antibody binding) set forth above.

3. Applicant argument that Pirrung still requires labeled materials in contrast to the claimed invention that does not require the constraint of labeling. Applicant directs the examiner attention to page 35 of Pirrung. This argument have been fully considered but not found to be persuasive.

In response, although applicant argues the option of not using labeling in the detection method, this limitation is not found in the instant claimed invention and therefore the claims have not been distinguished over the prior art already cited.

4. Applicant argues that that the reference does not teach how X-ray fluorescence would be combined with the teachings of Pirrung. This argument have been fully considered but is moot in view of the newly applied reference of Wang that teaches detection of antigen and antibody binding using X-ray fluorescence set forth above.

5. Applicant argues that the method step of Pirrung and what is claimed does not happen in the correct order. Applicant specifically points out that step 3 (the irradiation step) must occur after step 1 and step 2 and Pirrung does not meet this requirement. This argument have been fully considered but not found to be persuasive.

In response, it has been held that merely reversing the order of steps in a multi-step process is not a patentable modification absent unexpected or unobvious results. Ex parte Rubin, 128 U.S.P.Q. 440 (P.O.B.A. 1959). Cohn v. Comr. Patents, 251 F. Supp. 437, 148 U.S.P.Q. 486 (D.C. 1966).

6. Applicant have submitted evidence (i.e. two review articles) in support of X-ray fluorescence being non-obvious in evaluating chemical binding. Applicant declares that these articles were published two years after the instant patent application was filed concerning the same subject matter. The two articles and applicant arguments have been fully considered but not found to be persuasive in view of the newly secondary reference that teaches X-ray fluorescence for the detection of chemical binding between antigen and antibody as instantly claimed. Therefore, it is the position of the examiner that the cited references are prima facie obvious over the instant claims.

Conclusion

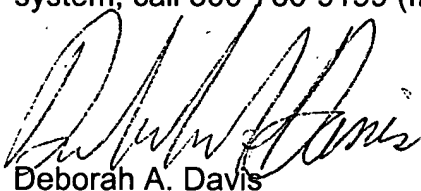
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A. Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, McKelvey Terry can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Deborah A. Davis
Patent Examiner
September 2006



CHRISTOPHER R. TATE
PRIMARY EXAMINER